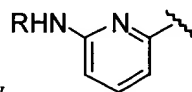


### III. REMARKS

Claims 8-16 are pending. To comply with the requirement for restriction, Claims 1-7 were withdrawn from consideration without prejudice to Applicant's right to file a divisional application directed to the subject matter therein. Claim 8 has been amended to become an independent claim to reflect the cancellation of Claim 1-7. The alternative language in the definition of  $Z_1 - Z_2$  in Claim 8 has been removed, and Markush language



added to provide proper claim form. The moiety has been removed.

Claim 9 has been amended to remove non-elected species. Claims 10, 11, 13, 15 and 16 were amended to reflect the cancellation of Claims 1-7. Claims 12 and 14 were amended to add the phrase " $\alpha_v\beta_5$  integrin-mediated" to further clarify and point out the invention, support for which can be found in Claims 11 and 13 from which 12 and 14 depend.

#### Declaration

On page 3 of the Office Action, the oath or declaration was alleged to be defective because the specification to which the declaration is directed was not adequately identified, and the citizenship of the fourth inventor was listed as R.O.C.. Attached herewith is an initialed copy of the fourth inventor's signature line with the country identified as R.O.C. spelled out as "Republic of China". Applicants submit that the declaration complies with the identification requirements of 37 C.F.R. 1.63. Applicants point out that MPEP 602 recites the following as compliance with any one of the items listed as acceptable for compliance with the identification requirement of 37 C.F.R. 1.63: (1) name of inventor(s) + reference to an attached specification; (2) name of inventor(s) + the attorney docket number of the specification as filed; or (3) name of inventor(s) + the title of the invention which was on the specification as filed. Applicants submit that the Declaration filed for the present invention contained both (2) (names of inventors + 3285US docket number) and (3) (names of inventors + "Bicyclic Alpha-v Beta-3 Antagonists" title. Therefore, the specification is adequately identified, and Applicants respectfully request that the objection be withdrawn.

#### Restriction Requirement

Applicants affirm the election without traverse to prosecute the invention of Example 10 where ring A-B forms a 1-oxo-isoquinoline ring system.

### Co-Pending Applications

Applicants direct the Office's attention to the following co-pending U.S. applications, without conceding the materiality of the co-pending applications to the present invention:

- US 10/363070 (national phase of the PCT claiming priority from the same provisional application as the present invention)

### Rejections

*Rejection under 35 U.S.C. § 112, first paragraph*

#### **A. Claims 10-16 are enabled.**

On pages 5-6 of the Office Action, the Office rejected Claims 10-16 for lack of enablement of treatment of "cancer" generally. Applicants point out that the claims are not directed to not "cancer" generally.

- Claim 10 is directed to a pharmaceutical composition, which Applicants point out has been enabled by pages 27-28 of the specification.
- Claim 16 is directed towards a compound that selectively antagonizes the  $\alpha_v\beta_3$  and the  $\alpha_v\beta_5$  integrins, over the  $\alpha_v\beta_6$  integrin, enabled by pages 104-110 of the specification.
- Claims 11 and 13 provide for methods for treating conditions mediated by the  $\alpha_v\beta_3$  and  $\alpha_v\beta_5$  integrins, respectively. Claims 12 and 14 are dependent on claims 11 and 13. Claims 12 and 14 have been amended to make explicit this dependency. Further, the claims are directed towards the treatment of tumor metastasis, tumor growth and solid tumor growth, and not cancer generally. Therefore, the claims are directed towards a method for treating  $\alpha_v\beta_3$  mediated-tumor metastasis in a mammal, a method for treating  $\alpha_v\beta_5$  mediated-tumor angiogenesis and a method for treating  $\alpha_v\beta_5$  mediated-solid tumor growth or solid tumor growth in a mammal, respectively. Further, the claims are directed towards a *treatment* of tumor metastasis or tumor growth, not a cure for cancer. Also, Applicants set out the dose ranges and administration of the compounds of the present invention are given on page 29 of the specification, and the enzyme selectivity assays are given in the Examples. Those skilled in the art of treatment, i.e., oncologists, have a high level of education and skill, and have the ability to

select dose ranges for treatment. Therefore, one of ordinary skill could practice the invention without an undue burden using the specification in light of what was known in the art.

- Claim 15 is directed towards a combination therapy with known chemotherapeutic agents. Applicants submit that the standard treatment of various solid tumors using various chemotherapeutic agents is well-known in the art (see, for example, Lippincott's Cancer Chemotherapy Handbook, Delia C. Baquiran and Jean Gallagher, Lippincott Williams & Wilkins Publishers; 1st edition (January 15, 1998)). Further, examples and doses of such chemotherapeutic agents are given on pages 31-33 of the specification. Therefore, no undue experimentation required by one of skill to combine the standards of treatment for a given neoplasia and the compounds of the present invention.

*Rejection under 35 U.S.C. § 112, second paragraph*

**A. Dependency of Claim 8**

The “1-oxo-isoquinoline” limitation in Claim 8 was rejected as lacking antecedent basis. Claim 8 has been re-written to be an independent claim, support for which can be found on page 14, lines 1-5.

**B. Definitions of “B”**

The terms “B” Claims 3 and 8 were rejected as having multiple definitions. Claim 8 has been amended to include B<sup>1</sup>- B<sup>7</sup>. To comply with the requirement for restriction, Claim 3 was withdrawn from consideration without prejudice to Applicant’s right to file a divisional application directed to the subject matter therein.

**C. Definitions of “R”**

The terms “R” Claims 3 and 8 were rejected as having multiple definitions. Claim 8 has been amended to include R<sup>79</sup>- R<sup>81</sup>. To comply with the requirement for restriction, Claim 3 was withdrawn from consideration without prejudice to Applicant’s right to file a divisional application directed to the subject matter therein.

**D. Definitions of “X”**

The terms “X” Claims 3 and 8 were rejected as having multiple definitions. Claim 8 has been amended to include X<sup>7</sup>- X<sup>8</sup>.

**E. Dependency of Claim 8**

The “n= 1 or 2” limitation in Claim 8 was rejected as lacking antecedent basis. Claim 8 has been re-written to be an independent claim, support for which can be found on page 14-15. The term “n” has been amended to “m” to more specifically point out the invention.

**F. Definiteness of Claim 9**

Claim 9 was rejected for indefiniteness for containing an open bracket. Claim 9 has been amended to include the bracket XXX, support for which can be found on XXX.

**G. Definiteness of Claims 10-16**

Claims 10-16 were rejected for alleged indefiniteness because, according to the Office, it would require undue experimentation to determine the scope of the claims. Since this rejection relies on the argument that the claims are non-enabled, and Applicants have shown the enablement of the claims above, the rejection is rendered moot.

**H. Definiteness of Claim 15**

On page 10 of the Office Action, the Office rejects Claim 15 for the alleged indefiniteness of the term “chemotherapeutic agent”. Applicants submit that the term “chemotherapeutic agent” is well-known in the art, (see, for example, Lippincott's Cancer Chemotherapy Handbook, Delia C. Baquiran and Jean Gallagher, Lippincott Williams & Wilkins Publishers; 1st edition (January 15, 1998)). Further, examples and doses of such chemotherapeutic agents are given on pages 31-33 of the specification.

**I. Claim 16**

Claim 16 was rejected for allegedly being a substantial duplicate of Claims 8-9. Applicants submit that the term “that selectively antagonizes the  $\alpha_v\beta_3$  and the  $\alpha_v\beta_5$  integrins, over the  $\alpha_v\beta_6$  integrin” is not, as suggested by the Office, an inherent use, but rather is a further limitation to those compounds of Claims 1-9 that are observed to have the property. Therefore, the scope of the claims is different, and they are not duplicative.

*Rejections under 35 U.S.C. § 102*

**A. WO 97/24119 does not anticipate amended Claims 8 and 10-16**

On page 10 of the Office Action, Claims 8 and 10-16 were rejected as allegedly being anticipated by Miller *et al* (WO 97/24119), example 76. Applicants point out that example 76 in Miller *et al*. differs from the amended claim 8 in that that the moiety A<sup>1</sup>

does not include the methyl benzimidazol as shown in Miller. Therefore, Applicants request that the rejection be withdrawn.

**B. WO 97/24122 does not anticipate amended Claims 8 and 10-16**

On page 10 of the Office Action, Claims 8 and 10-16 were rejected as allegedly being anticipated by Ali *et al* (WO 97/24122), example 28. Applicants point out that example 28 in Ali *et al*. differs from the amended claim 8 in that the moiety A<sup>1</sup> does not include the methyl benzimidazol as shown in Ali. Therefore, Applicants request that the rejection be withdrawn.

It is therefore submitted that Claims 1-16 are in condition for allowance. If the Office has any further comments or concerns, the Examiner is welcome to contact Applicants at the number below.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Rachel A. Polster', written in a cursive style.

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